

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE

IN RE: '318 PATENT INFRINGEMENT	)	
LITIGATION	)	
	)	C.A. No. 05-356-KAJ
	)	(consolidated)
	)	
	)	

**REQUEST FOR JUDICIAL ASSISTANCE FOR THE PURPOSE OF  
OBTAINING EVIDENCE AND ORAL EXAMINATIONS  
UNDER OATH PURSUANT TO THE HAGUE CONVENTION OF  
18 MARCH 1970 ON THE TAKING OF EVIDENCE ABROAD IN CIVIL OR  
COMMERCIAL MATTERS (BOEHRINGER INGELHEIM GMBH AND CO. KG)**

From the People of the United States of America, to the Central Authority - Rhineland-  
Palatinate, Das Ministerium der Justiz, Ernst-Ludwig-Strasse 3, 55116 Mainz, Germany,

GREETINGS:

- |    |   |   |
|----|---|---|
| 1. | Sender  | United States District Court<br>District of Delaware<br>J. Caleb Boggs Federal Building<br>844 N. King Street<br>Wilmington, DE 19801<br>United States of America   |
| 2. | Central Authority of the<br>Requested State:              | Central Authority - Rhineland-Palatinate<br>Das Ministerium der Justiz<br>Ernst-Ludwig-Strasse 3<br>55116 Mainz, Germany  |
| 3. | Person to whom the executed<br>request is to be returned: | ASHBY & GEDDES<br>Steven J. Balick (Delaware Bar No. 2114)<br>John G. Day (Delaware Bar No. 2403)<br>222 Delaware Avenue<br>17th Floor<br>P.O. Box 1150<br>Wilmington, DE 19899<br>Telephone: 302-654-1888<br>Facsimile: 302-654-2067<br>Email: sbalick@ashby-geddes.com<br>jday@ashby-geddes.com |

4. Specification of the date by which the requesting authority requires receipt of the response to the Letter of Request

Date: June 14, 2006

IN CONFORMITY WITH ARTICLE 3 OF THE CONVENTION, THE UNDERSIGNED APPLICANT HAS THE HONOR TO SUBMIT THE FOLLOWING REQUEST:

5. a. Requesting Judicial Authority: United States District Court  
District of Delaware  
J. Caleb Boggs Federal Building  
844 N. King Street  
Wilmington, DE 19801
- b. To the competent authority of the Central Authority - Rhineland-Palantinate  
Das Ministerium der Justiz  
Ernst-Ludwig-Strasse 3  
55116 Mainz, Germany
- c. Name of the case and any identifying number In re: '318 Patent Infringement Litigation,  
C.A. No. 05-356-KAJ (consolidated)
6. Names and addresses of the parties and their representatives:
- a. Plaintiffs: Janssen Pharmaceutica N.V.  
Turnhoutseweg 30  
2340 Beerse, Belgium
- Janssen, L.P.  
1125 Trenton Harbourn Road  
PO Box 200  
Titusville, NJ 08560
- Synaptech, Inc.,  
P.O. Box 157  
Cold Spring Harbor, NY 11724
- Representatives:  
Steven J. Balick  
John G. Day  
ASHBY & GEDDES  
222 Delaware Avenue  
17th Floor

P.O. Box 1150  
Wilmington, DE 19899  
Tel: 302.654.1888  
Fax: 302.654.2067

Steven P. Berman  
JOHNSON & JOHNSON  
Office of General Counsel  
One Johnson & Johnson Plaza  
New Brunswick, NJ 08933

b. Defendants:

- 1) Teva Pharmaceuticals USA  
1090 Horsham Road  
North Wales, PA 19454

Teva Pharmaceuticals Industries, Ltd.  
5 Basel St.  
Petach Tikva 49131  
Israel

Representatives:

Josy W. Ingersoll  
John W. Shaw  
Adam W. Poff  
YOUNG CONAWAY STARGATT & TAYLOR LLP  
The Brandywine Building  
1000 West Street  
17th Floor  
Wilmington, DE 19899-0391  
Phone: 302.571.6600  
Fax: 302.571.1253

Daniel F. Attridge, P.C. (dattridge@kirkland.com)  
Edward C. Donovan (edonovan@kirkland.com)  
Karen M. Robinson (krobinson@kirkland.com)  
Corey J. Manley (cmanley@kirkland.com)  
KIRKLAND & ELLIS LLP  
655 Fifteenth Street, NW  
Suite 1200  
Washington, DC 20005-5793  
Phone: 202.879.5000  
Fax: 202.879.5200

- 2) Mylan Pharmaceuticals Inc.  
781 Chestnut Ridge Rd.  
Morgantown, WV 26505

Mylan Laboratories, Inc  
1500 Corporate Drive  
Suite 400  
Canonsburg, PA15317

Representatives:

Mary B. Matterer  
MORRIS JAMES HITCHENS & WILLIAMS LLP  
222 Delaware Avenue  
10th Floor  
P.O. Box 2306  
Wilmington, DE 19899-2306  
Phone: 302.888.6800  
Fax: 302.571.1750

William A. Rakoczy  
Christine J. Siwik  
Amy D. Brody  
RAKOCZY, MOLINO, MAZZOCHI, SIWIK LLP  
6 West Hubbard Street, Suite 500  
Chicago, IL 60610  
Phone: 312.527.2157  
Fax: 312.527.4205

- 3) Barr Laboratories  
223 Quaker Road  
Pomona, NY 10970

Barr Pharmaceuticals, Inc.  
400 Chestnut Ridge Rd.  
Woodcliff Lake, NJ 07677-7668

Representatives:

John C. Phillips Jr.  
Brian E. Farnan  
PHILLIPS GOLDMAN & SPENCE, P.A.  
1200 N. Broom Street  
Wilmington, DE 19806  
Phone: 302.655.4200  
Fax: 302.655.4210

George C. Lombardi  
Taras A. Gracey  
Lynn M. Ulrich  
WINSTON & STRAWN LLP  
35 West Wacker Drive  
Chicago, IL 60601  
Phone: 312.558.5600

Fax: 312.558.5700

- 4) Purepac Pharmaceutical Co  
14 Commerce Dr., Ste. 301  
Cranford, NJ 07016

Alpharma, Inc.  
1 Executive Dr.  
Fort Lee, NJ 07024

Representatives:

Richard D. Kirk  
THE BAYARD FIRM  
222 Delaware Avenue, Suite 900  
P.O. Box 25130  
Wilmington, DE 19899  
Phone: 302.655.5000  
Fax: 302.658.6395

Robert J. Gunther, Jr. (robert.gunther@lw.com)  
James P. Barabas (james.barabas@lw.com)  
LATHAM & WATKINS LLP  
885 Third Avenue, Suite 1000  
New York, NY 10022-4834  
Phone: 212.906.1200  
Fax: 212.751.4864

- 5) Dr. Reddy's Laboratories, Inc.  
200 Somerset Corp. Blvd.  
Bridgewater, NJ 08807

Dr. Reddy's Laboratories, Ltd.  
7-1-27, Ameerpet  
Hyderabad, Andhra Pradesh 500 016, India

Representatives:

Richard L. Horwitz  
David E. Moore  
POTTER ANDERSON & CORROON LLP  
Hercules Plaza, 6th Floor  
1313 N. Market Street  
PO Box 951  
Wilmington, DE 19899  
Phone: 302.984.6000  
Fax: 302.658.1192

Stuart Sender  
BUDD LARNER, P.C.  
150 John F. Kennedy Parkway  
Short Hills, NJ 07078-0999  
Phone: 973.315.4462  
Fax: 973.379.7734

- 6) Alphapharm Pty Ltd.  
Chase Building 2, 1 Wentworth Park Road  
Glebe NSW 2037  
Australia

Representatives:

Frederick L. Cottrell, III  
Anne Shea Gaza  
RICHARDS, LAYTON & FINGER, P.A.  
One Rodney Square  
P.O. Box 551  
Wilmington, DE 19899  
Phone: 302.651.7700  
Fax: 302.651.7701

Alan Bernstein  
Mona Gupta  
CAESAR, RIVISE, BERNSTEIN, COHEN &  
POKOTILOV, LTD.  
1635 Market Street, 11th floor  
Philadelphia, PA 19103-2212  
Phone: 215.567.2010  
Fax: 215.751.1142

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|----|----|--|--|
| 7. | a. | Nature of the Proceedings<br>(divorce, paternity, breach<br>of contract, product<br>liability, etc.) | This consolidated action is for patent infringement<br>arising under the patent laws of the United States,<br>Title 35 of the United States Code, for infringement<br>of United States Patent No. 4,663,318 ("the '318<br>patent") attached hereto as Exhibit 1. |
|----|----|--|--|

- b. Summary of Complaint Plaintiffs are exclusive licensees under the '318 patent, pursuant to an exclusive license agreement between Synapttech and Ms. Bonnie M. Davis, Ph.D, Janssen Pharmaceutica N.V., and Janssen Pharmaceutica Products, L.P., of the right to make, use and sell certain pharmaceutical preparations containing galanthamine hydrobromide to treat Alzheimer's Disease in the United States and other territories. Pursuant to that exclusive license, Plaintiffs currently market galanthamine hydrobromide tablets under the trademark RAZADYNE®. Until 2005, Plaintiffs market galanthamine hydrobromide tablets for the purpose of treating Alzheimer's disease under the trademark REMINYL®. As exclusive licensees, Plaintiffs are authorized to enforce the '318 patent.
- Defendants submitted Abbreviated New Drug Applications (ANDAs) to the Food and Drug Administration seeking approval to engage in the commercial manufacture, use, offer for sale and sale of galanthamine hydrobromide tablets before the expiration of the '318 patent.
- Plaintiffs seek judgment declaring that the making, using, selling, offering to sell, or importing of the galanthamine hydrobromide described Defendants' ANDAs constitute infringement of the '318 patent, or inducing or contributing to such conduct.
- c. Summary of defense and counterclaim. On December 2, 2005, the parties entered into a Stipulation Not to Contest Infringement of the asserted claims of the '318 patent (claims 1 and 4). Defendants continue to assert that these claims are invalid. For example, Defendants contend that the asserted claims of the '318 patent are obvious to one of ordinary skill in the art and/or anticipated by prior art (prior published work) and seek as counterclaims judgment of invalidity of the asserted claims of the '318 patent.
- d. Other necessary information or documents To establish validity of a patent, U.S. law requires the courts to consider objective considerations of non-obviousness to establish that the patent was not obvious. These objective considerations of nonobviousness include skepticism of the invention by those who rejected opportunities to license the invention based on a belief that it was not effective and

the long felt by the community and companies for the invention.

8. a. Evidence to be obtained or other judicial act to be performed:
  - 1) The names of all persons employed by Boehringer Ingelheim KG who were involved in any evaluation, consideration of discussion to license, market or develop the '318 patent or a '318 patent product.
  - 2) The names and responsibilities of all persons employed by Boehringer Ingelheim KG who were involved in any evaluation, consideration, or discussion of galanthamine as a treatment for dementia of the Alzheimer's type.
  - 3) All negotiations of communications between Boehringer Ingelheim KG and Synpatech or Dr. Bonnie Davis regarding galanthamine as a treatment for dementia of the Alzheimer's type.
  - 4) Information related to the November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that "based on our extensive preclinical research data available to us, it is our feeling that this compound, while interesting from the point of view of its mechanism of action (acetylcholinesterase inhibitor), does not have the biochemical and pharmacological profile which we consider essential for its potential use in the treatment of Alzheimer's disease."
  - 5) Information related to the November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that "[t]he limited clinical data (pilot study by Michael Rainer) are not very convincing."
  - 6) Information related to the Confidentiality Agreement dated November 10, 1989, attached hereto as Exhibit 3.
  - 7) Production of all documents relevant to (3) - (6) and deposition upon oral examination of Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG or a corporate representative of Boehringer Ingelheim KG;
  - 8) Authentication of Exhibits 2 and Exhibit 3.



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|-----|--|---|
| b.  | Purpose of the evidence or judicial act sought                         | The purpose of this request for documents is to obtain trial evidence necessary to prove the validity of the '318 patent  |
| 9.  | Identity and address of persons to be examined:                        | <p>1) Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG</p> <p>2) A corporate representative of Boehringer Ingelheim most knowledgeable to the issues set forth in Section 8.</p>  |
|     | Requested time and place of examination:                               | <p>Production of documents to be received by May 31, 2006.</p> <p>Deposition to occur at 9:00 a.m. at the U.S. Consulate in Frankfurt, Germany on June 14, 2006.</p> <p>Or such other date, time and/or venue as determined by the Court.</p>   |
| 10. | Statement of subject matter about which the witness is to be examined: | <p>Each of the individuals is to be examined about the following subject matter:</p> <p>1) The names of all persons employed by Boehringer Ingelheim KG who were involved in any evaluation, performed: consideration of discussion to license, market or develop the '318 patent or a '318 patent product.</p> <p>2) The names and responsibilities of all persons employed by Boehringer Ingelheim KG who were involved in any evaluation, consideration, or discussion of galanthamine as a treatment for dementia of the Alzheimer's type.</p> <p>3) All negotiations of communications between Boehringer Ingelheim KG and Synpatech or Dr. Bonnie Davis regarding galanthamine as a treatment for dementia of the Alzheimer's type.</p> <p>4) The November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that "based on our extensive preclinical research data available to us, it is our feeling that this compound, while interesting from the point of view of its mechanism of action</p> |

(acetylcholinesterase inhibitor), does not have the biochemical and pharmacological profile which we consider essential for its potential use in the treatment of Alzheimer's disease."

5) The November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that "[t]he limited clinical data (pilot study by Michael Rainer) are not very convincing."

6) The Confidentiality Agreement dated November 10, 1989, attached hereto as Exhibit 3.

11. Documents or other property to be inspected:

It is requested that Boehringer Ingelheim KG produce the following documents for copying and inspection:

1) All negotiations of communications between Boehringer Ingelheim KG and Synpatech or Dr. Bonnie Davis regarding galanthamine as a treatment for dementia of the Alzheimer's type.

2) All Documents related to the November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that "we have given serious consideration to the proposal of Waldheim Pharmazeutika to develop Nivalin (galanthamine) for the indication Alzheimer's disease."

3) All documents related to the November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that "based on our extensive preclinical research data available to us, it is our feeling that this compound, while interesting from the point of view of its mechanism of action (acetylcholinesterase inhibitor), does not have the biochemical and pharmacological profile which we consider essential for its potential use in the treatment of Alzheimer's disease."

4) All documents related to the November 8, 1989, letter from Prof. E. Muller, Department of Pharmacology, Boehringer Ingelheim KG, attached

hereto as Exhibit 2 including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statements set forth in the letter that “[t]he limited clinical data (pilot study by Michael Rainer) are not very convincing.”

5) All documents related to the Confidentiality Agreement dated November 10, 1989, attached hereto as Exhibit 3.

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|--|--|
| 12. Any requirement that the evidence be given on oath or affirmation and any special form to be used:                                   | It is required that the oral examinations be conducted under oath or affirmation. In the event that the evidence cannot be taken in the manner requested, it is requested that the evidence be taken in such manner as provided by local law for the formal taking of evidence.  |
| 13. Special methods or procedures to be followed:  | It is requested that the witness be placed under oath (or affirmation) that counsel for all parties be permitted to question the witness and that all questions and answers be transcribed by a shorthand typist as well as videotaped by a videographer. It is requested that insofar as it is not incompatible with the laws of Germany, the rules of procedure governing the taking of depositions in the United States be applied. |
| 14. Request for notification of the time and place for the execution of the Letter of Request  | Under Article 7, it is requested that notification be sent directly to each party’s representative(s).   |
| 15. Request for attendance or participation of judicial personnel of the requesting authority at the execution of the Letter of Request: | Not requested.   |
| 16. Specification of privilege or duty to refuse to give evidence under the law of the State of Origin:                                  | None.  |
| 17. The fees and costs incurred which are reimbursable will be borne by:   | ASHBY & GEDDES<br>Steven J. Balick (Delaware Bar No. 2114)<br>John G. Day (Delaware Bar No. 2403)<br>222 Delaware Avenue<br>17th Floor<br>P.O. Box 1150<br>Wilmington, DE 19899  |

Telephone: 302-654-1888

Facsimile: 302-654-2067

18. Date of Request

April \_\_\_\_\_, 2005

19. Signature and seal of the  
requesting Authority:

By the Court:

By:

\_\_\_\_\_  
United States District Judge for  
the District of Delaware

169034.1

# EXHIBIT 1

**United States Patent** [19]  
**Davis**

[11] **Patent Number:** 4,663,318  
[45] **Date of Patent:** May 5, 1987

[54] **METHOD OF TREATING ALZHEIMER'S DISEASE**

[76] **Inventor:** Bonnie Davis, 17 Seacrest Dr.,  
Huntington, N.Y. 11743

[21] **Appl. No.:** 819,141

[22] **Filed:** Jan. 15, 1986

[51] **Int. Cl.:** ..... A61K 31/55

[52] **U.S. Cl.:** ..... 514/215

[58] **Field of Search** ..... 514/215

[56] **References Cited**  
**PUBLICATIONS**

Chem. Abst. (81)-72615z (1974).  
Chem. Abst. (86)-115157z (1977).

Horshenson et al. J. Med. Chem. vol. 29, No. 7, 7/86,  
pp. 1125-1130.

Kendall et al., J. Chem. & Hospital Pharmacol., (1985)  
10-327-330.

S. Chaplygina et al., J. of Highest Nervous Activity vol.  
XXIV 1976 Issue 5, pp. 1-4.

Krause, J. of Highest Nervous Activity, vol. XXII,  
1974, Issue 4.

*Primary Examiner*—Stanley J. Friedman  
*Attorney, Agent, or Firm*—Ladas & Parry

[57] **ABSTRACT**

Alzheimer's disease may be treated with galanthamine.

7 Claims, No Drawings

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## METHOD OF TREATING ALZHEIMER'S DISEASE

### GENERAL FIELD OF THE INVENTION

The present invention relates to a novel method of treating Alzheimer's disease and more particularly to a treatment using galanthamine.

### BACKGROUND ART

Galanthamine and acid addition salts thereof have, for many years, been known to have anticholinesterase properties. Cozanitis in *Anaesthesia* 29 163-8 (1974) describes the effect of galanthamine hydrobromide on plasma cortisol of patients receiving relaxant anaesthesia and Cozanitis et al in *Acta Anesth. Scand.* 24:166-168 (1980) describe the effect of galanthamine on plasma ACTH values during anaesthesia. These studies showed an increase in both plasma cortisol and plasma ACTH when galanthamine was administered to patients together with atropine.

Il'yuchenok et al (Chemical Abstracts 70 36296K) describe the appearance of  $\theta$ -rhythm on an electroencephalogram when galanthamine is administered intravenously to rabbits.

Increase in short-term memory in dogs by use of galanthamine is described by Krauz in Chemical Abstracts 81 72615Z.

The antagonistic effect of galanthamine to scopolamine-induced amnesia in rats is described by Chaplygina et al in Chemical Abstracts 86 115157Z, and in *Zhurnal Vysshei Nervnoi Deiatelnosti imeni P. Pavlova (MOSKVA)* 26:1091-1093, 1976.

Alzheimer's disease, presenile dementia, causes much distress not only to those suffering from the disease, but also those who are close to them. The custodial care of advanced victims of the disease is a tremendous expense to society. At present, there is no effective means of improving the functional status of persons with the disease.

It is an object of the present invention to improve the cognitive function of patients with Alzheimer's disease.

### SUMMARY OF THE INVENTION

A method for treating Alzheimer's disease and related dementias which comprises administering to mammals, including humans, an effective Alzheimer's disease cognitively-enhancing amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof. A radioactively-labelled form of the molecule may also serve as a diagnostic test for Alzheimer's disease.

### DETAILED DESCRIPTION OF THE INVENTION

Galanthamine can be administered in any convenient chemical or physical form. For example, it may be administered as its hydrobromide, hydrochloride, methylsulfate or methiodide.

Galanthamine or its pharmaceutically-acceptable acid addition salts may be administered to a patient suffering from Alzheimer's disease orally or by subcutaneous or intravenous injection, or intracerebroventricularly by means of an implanted reservoir. It may be necessary to begin at lower doses than are ultimately effective.

Galanthamine and its acid addition salts form crystals. They are in general only sparingly soluble in water

at room temperature and so injectible compositions are normally in the form of an aqueous suspension. If necessary, pharmaceutically-acceptable suspension aids may be employed. Typically, such a suspension will be employed at a concentration of 1-50 mg/ml more commonly 5-40 mg/ml, for example, 5-30 mg/ml or 10-40 mg/ml, typically 20-30 mg/ml of galanthamine. Typical dosage rates when administering galanthamine by injection are in the range 5-1,000 mg per day depending upon the patient. For example, divided doses in the range 0.5-5 mg/kg body weight per day may prove useful. Typically, one might administer a dosage of 50-300 mg per day to a patient of a body weight of 40-100 kg, although in appropriate cases such dosages may prove useful for patients having a body weight outside this range. In other cases, dosages as low as 10 mg and as high as 500 mg may be appropriate for persons in this body weight range.

Galanthamine or its pharmaceutically-acceptable acid addition salts may also be administered orally, for example, as an aqueous suspension or a solution in aqueous ethanol or as a solid such as a tablet or capsule. Suspensions or solutions for oral administration are typically of about the same concentration as those used for injections. However, it may be desirable when administering the drug orally to use a higher dosage rate than when administering it by injection. For example, dosages up to 2000 mg per day may be used, such as dosages in the range 100-600 mg per day. In preparing such tablets or capsules, standard tablet or capsulemaking techniques may be employed. The dosage rate of galanthamine or its pharmaceutically-acceptable salt will normally be in the same range as for oral administration of a liquid. If desired, a pharmaceutically-acceptable carrier such as starch or lactose may be used in preparing galanthamine tablets. Capsules may be prepared using soft galatine as the encapsulating agent. If desired, such capsules may be in the form of sustained release capsules wherein the main capsule contains microcapsules of galanthamine which release the contents over a period of several hours thereby maintaining a constant level of galanthamine in the patient's blood stream.

The following test provides a good animal model for Alzheimer's disease in humans: A selective lesion is placed in a subcortical nucleus (nucleus basalis of Meynert) with a resultant cortical cholinergic deficiency, similar in magnitude to that seen in early to moderate stage Alzheimer's disease. Numerous behavioral deficits, including the inability to learn and retain new information, characterizes this lesion. Drugs that can normalize these abnormalities would have a reasonable expectation of efficacy in Alzheimer's disease. Haroutunian, V, Kanof P, Davis, KL: Pharmacological alleviations of cholinergic-lesion-induced memory defects in rats. *Life Sciences* 37:945-952, 1985.

The following specific formulations may find use in treatment of Alzheimer's disease:

Tablets or capsules containing 5, 10 and 25 mg galanthamine hydrobromide to be taken four times a day, or a sustained-release preparation delivering an equivalent daily dose.

Parenteral solution containing 5 mg/ml.

Liquid formulation for oral administration available in 5 mg/5 ml and 25 mg/5 ml concentration.

There have been reports that galanthamine can cause cardiac arrhythmias. In such cases, it may be desirable to

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administer galanthamine in conjunction with another drug such as propanthelinbromide to control such arrhythmias.

I claim:

1. A method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

2. A method according to claim 1, wherein the administration is parenteral at a daily dosage of 5-1,000 mg of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

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3. A method according to claim 2, wherein said dosage rate is 50-300 mg per day.

4. A method according to claim 1, wherein said administration is oral and is in the range 10-2000 mg per day.

5. A method according to claim 4, wherein said dosage rate of 100-600 mg per day.

6. A method according to claim 1, wherein galanthamine is administered at a dosage rate of 0.1 to 4 mg/kg body weight of a patient, parenterally.

7. A method according to claim 1, wherein galanthamine is administered intracerebroventricularly via an implanted reservoir at a dosage rate of 0.01 to 5.0 mg/kg day.

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# **EXHIBIT 2**

# Boehringer Ingelheim



Boehringer Ingelheim KG - 6507 Ingelheim am Rhein

Boehringer Ingelheim KG

Prof. Dr. P. Placheta  
Bender & Co. Ges.m.b.H.  
Dr.-Boehringer-Gasse 5 - 11  
A-1120 Wien

Ihr Zeichen      Ihre Nachricht vom      Unser Zeichen      Telefon-Durchwahl      6507 Ingelheim am Rhein,  
Dr. Mü-ra      06132-77-4194      den November 8., 1989

Dear Prof. Placheta,

we have given serious consideration to the proposal of Waldheim Pharmazeutika to develop Nivalin (galanthamine) for the indication Alzheimer's disease. Based on the extensive preclinical research data available to us, it is our feeling that this compound, while interesting from the point of view of its mechanism of action (acetylcholinesterase inhibitor), does not have the biochemical and pharmacological profile which we consider essential for its potential use in the treatment of Alzheimer's disease. The limited clinical data (pilot study by Michael Rainer) are not very convincing.

Furthermore, Dr. Bonnie Davis has already applied for a patent to use galanthamine in AD-patients in the US and several other countries. To my knowledge, this patent has been granted and Waldheim Pharmazeutika is well aware of this.

We would, therefore, not recommend that Boehringer should get involved in the development of Nivalin for the treatment of Alzheimer's disease.

With best regards

BOEHRINGER INGELHEIM KG  
ppa.

i. V.

Dr. M. Herschel  
(Dept. of Medicine)

*Müller*  
Prof. E. Müller  
(Dept. of Pharmacology)

cc.: Prof. Jennewein  
Dr. Bachtler  
Dr. Heil

Dr. Bonnie Davis  
(Mount Sinai Medical Center, N.Y.)

Geschäftsführung: Hans-Jörg Gausler, Vorsitzender · Werner Hoffmann · Dr. Heribert Johann · Dr. Eberhard Kuster · Dr. Helmut Rodmann  
Ingelheim 6507 77-0  
Kfz 4167910 dx d  
Boehringer Ingelheim Rhein  
Fax 77-3080

Deutsche Bank AG, Mainz 0 102 221 (BLZ 550 400 40)  
Dresdner Bank AG, Mainz 248 569 700 (BLZ 550 600 85)  
Landeszentralbank Mainz 55 907 367 (BLZ 550 000 00)

Kreisbank Bingen 1008 300 (BLZ 552 600 10)  
Postbank Frankfurt/Main 1653-602 (BLZ 500 100 60)

0551-KG

# **EXHIBIT 3**

16 NOV. '89 09:49 BI KG PHARMKOLOGIE 0000

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## IDENTIALITY AGREEMENT

of November 1989, this agreement, made this 10<sup>th</sup> day of November, 1989, by and between Dr. B. Davis (hereinafter referred to as "bjm"), and Boehringer Ingelheim Corporation, of Ridgefield, Connecticut and West Germany, (hereinafter referred to as "BI")

~~\* International GmbH \* KG~~  
WITNESSETH

Whereas, bjm possesses certain confidential trade secret information, data and know-how relating to products for the treatment of Alzheimer's disease and related dementias ("product"); and

Whereas, BI wishes to receive said confidential trade secret information, data and know-how for the purpose of evaluating same to determine its commercial interest therein; and

Whereas, bjm is agreeable to providing BI with said information upon the terms and conditions as stated hereinafter,

Now, therefore, in consideration of the foregoing mutual premises and mutual covenants recited herein, the parties hereto agree as follows:

1. "Confidential information", as used herein, means any and all information relating to the product furnished by bjm to BI, either directly or indirectly, with the exception only of the following:

(a) information that as of the date of receipt by BI is publicly available or subsequently becomes so without fault on the part of BI;

(b) information that at the time of receipt by BI was known to it from its own sources;

(c) information that at any time is received in good faith by BI from a third party that was lawfully in possession of the same and had the right to disclose the same; and

(d) information that the parties hereto mutually agree to release from the terms of this agreement.

2. Promptly following execution of this Agreement, bjm shall provide BI with such information that bjm has in its possession relating to the product as may be necessary and sufficient for BI to determine its commercial interest therein.

3. BI agrees to receive and maintain in confidence all Confidential information to no one other than its officers and employees or governmental regulatory officials who are directly concerned with its evaluation, and shall take all reasonable precautions to prevent the disclosure of Confidential information to any unauthorized person, firm, or company. Upon disclosing Confidential information to its officers and employees or governmental regulatory officials, BI shall advise said officers and employees of the confidential nature thereof, and shall use

reasonable efforts to prevent the unauthorized disclosure of such information by such officers and employees.

4. BI agrees not to use Confidential Information for any purpose other than the evaluation referred to in Paragraph 2 above without first obtaining the express written consent of bjm to do so or except pursuant to a further contractual arrangement between BI and bjm.

5. In the event BI does not wish to pursue product following its review, BI, at bjm's request, shall return all confidential information to bjm.

6. It is understood and agreed that the obligations of BI under this agreement shall continue for a period of ten (10) years from the date hereof, at the expiration of which period such obligations shall terminate.

7. It is understood that the obligations of BI under this agreement apply also to all other affiliates of BI.

IN WITNESS WHEREOF, each party hereto has caused this instrument to be executed, in duplicate, by its duly authorized representative as of the date first above written.

<sup>KG</sup>  
Boehringer Ingelheim Corporation  
~~Integrated~~  
By [Signature]  
Title PPA I.V.

Date Nov. 15, 1989

By [Signature]  
Bonnie M. Davis, M.D.

Date Nov. 10, 1989

**CERTIFICATE OF SERVICE**

I hereby certify that on the 28<sup>th</sup> day of April, 2006, the attached **REQUEST FOR JUDICIAL ASSISTANCE FOR THE PURPOSE OF OBTAINING EVIDENCE AND ORAL EXAMINATIONS UNDER OATH PURSUANT TO THE HAGUE CONVENTION OF 18 MARCH 1970 ON THE TAKING OF EVIDENCE ABROAD IN CIVIL OR COMMERCIAL MATTERS (BOEHRINGER INGELHEIM GMBH AND CO. KG)** was served upon the below-named counsel of record at the address and in the manner indicated:

John W. Shaw, Esquire  
Young Conaway Stargatt & Taylor, LLP  
The Brandywine Building  
1000 West Street, 17<sup>th</sup> Floor  
Wilmington, DE 19801

HAND DELIVERY

Daniel F. Attridge, P.C.  
Kirkland & Ellis LLP  
655 15<sup>th</sup> Street, N.W.  
Washington, DC 20005-5793

VIA FEDERAL EXPRESS

Mary B. Matterer, Esquire  
Morris James Hitchens & Williams LLP  
222 Delaware Avenue, 10<sup>th</sup> Floor  
Wilmington, DE 19801

HAND DELIVERY

William A. Rakoczy, Esquire  
Rakoczy Molino Mazzochi Siwik LLP  
6 West Hubbard Street, Suite 500  
Chicago, IL 60601

VIA FEDERAL EXPRESS

Richard L. Horwitz, Esquire  
Potter Anderson & Corroon LLP  
Hercules Plaza, 6<sup>th</sup> Floor  
1313 N. Market Street  
P.O. Box 951  
Wilmington, DE 19899

HAND DELIVERY

Stuart D. Sender, Esquire  
Budd Lerner, P.C.  
150 John F. Kennedy Parkway  
Short Hills, NJ 07078

VIA FEDERAL EXPRESS

John C. Phillips, Jr., Esquire  
Phillips, Goldman & Spence, P.A.  
1200 North Broom Street  
Wilmington, DE 19806

HAND DELIVERY

Lynn M. Ulrich, Esquire  
Winston & Strawn LLP  
35 West Wacker Drive  
Chicago, IL 60601

VIA FEDERAL EXPRESS

Richard D. Kirk, Esquire  
The Bayard Firm  
222 Delaware Avenue, Suite 900  
Wilmington, DE 19899

HAND DELIVERY

Robert J. Gunther, Jr., Esquire  
Latham & Watkins LLP  
885 Third Avenue, Suite 1000  
New York, NY 10022-4802

VIA FEDERAL EXPRESS

Frederick L. Cottrell, III, Esquire  
Richards, Layton & Finger  
One Rodney Square  
Wilmington, DE 19801

HAND DELIVERY

Alan H. Bernstein, Esquire  
Caesar, Rivise, Bernstein, Cohen & Pokotilow, Ltd.  
1635 Market Street, 12<sup>th</sup> Floor  
Philadelphia, PA 19103

VIA FEDERAL EXPRESS

Philip A. Rovner, Esquire  
Potter Anderson & Corroon LLP  
Hercules Plaza  
Wilmington, DE 19801

HAND DELIVERY

Barbara S. Wahl, Esquire  
Arent Fox PLLC  
1050 Connecticut Avenue, N.W.  
Washington, DC 20036-5339

VIA FEDERAL EXPRESS

*/s/ John G. Day*

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John G. Day